

REMARKS

Claims 26-47, 54, 55 and 59 are pending in the application.

Claims 26-47, 54 and 55 have been withdrawn. Of these claims 26-28, 31-34, 36-40, 42, 44, 46, 47 and 54 have been amended.

48-52 have been amended and new claim 59 has been added. Support for the amendments to the claims and new claim can be found through the specification and claims as originally filed.

Claims 53 and 56-57 have been cancelled without prejudice or disclaimer to the subject matter recited therein.

The amendments to the claims and the cancellations of claims are solely to advance prosecution. Applicants, by amending or cancelling any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert the original claim scope of any claim amended or cancelled herein, in a continuing application.

No new matter has been introduced to this application within the meaning of 35 U.S.C. §132.

Regarding the Examiner's comments with respect to the restriction requirement, Applicants acknowledge that the requirement has been made final. However, Applicants respectfully ask the Examiner to consider the fact that the claims in Groups I and II pertain to "chlorinated sucrose", even with additional impurities, the chemical identity of the product of Groups I and II is "chlorinated sucrose" only. The product

taught by Carolyn is identified as “sucralose-containing sweetener” or a meltable “blend of sucralose and acesulfame-K”. It is not identified as “sucralose and impurities”, and Applicants submit that no one in the art would identify the product of Carolyn as “crude sucralose”. The ingredients, other than sucralose, in a sweetener blend, which are added to achieve sweetness, i.e., Acesulfame-K, cannot be identified as “impurities”. Therefore, a sweetener or blend according to the teachings of Carolyn would not be viewed by a person skilled in the art as sucralose or “crude sucralose” according to the instant subject matter. Thus, the products identified in Groups I and II as compared to those taught by Carolyn are entirely different. They are two different products, i.e., “crude/impure chlorinated sucrose” versus a “sucralose containing sweetener” or a “blend of sucralose and acesulfame-K”. Hence, Applicants respectfully submit that the teachings of Carolyn provide an improper basis for finalizing the restriction requirement.

Furthermore, an essential element of claim 26 is “the liquids being obtained in a process of producing chlorinated sucrose, mainly 1',6' Dichloro-1',6'-Dideoxy-β- D-Fructo-Furanosyl-4-Chloro-4-Deoxy-α-D-Galactopyranoside”. This excludes any chemical compound that is not derived from the process of production instantly claimed. Applicants submit that the compositions taught by Carolyn are not obtainable by the process of drying of the instant claims. Additionally, the composition taught by Carolyn would not fall within the subject matter of claims 48-53, 57 and 58, because these claims are limited to 1',6' Dichloro-1',6'-Dideoxy-β- D-Fructo-Furanosyl-4-Chloro-4-Deoxy-α-D-Galactopyranoside.

Claim 1 has been further amended to clarify that sucralose formed has at a least part of which is amorphous or non crystalline; and this is another factor that clarifies unity of invention between the Group I and Group II claims.

For at least these reasons, Applicants respectfully request reconsideration of the finality of restriction requirement.

I. Claim Objections

In the Action, the Examiner objected to claims 48-53, 57 and 58 as being dependent upon withdrawn claims. Applicants respectfully submit that the claims have been amended or -cancelled to overcome this objection, which is respectfully requested to be withdrawn.

II. Rejections under 35 U.S.C. §112

A. First Paragraph - Enablement

In the Action, the Examiner has rejected claims 48-53, 57 and 58 for lack of enablement.

Applicants traverse this rejection.

The phrase "substantially pure form" is not used in claims 48-53, 57 and 58, and as currently amended, the phrase is not a subject of the rejected claims.

With respect to the Examiner's comments regarding the potential indefiniteness of "substantially pure form", Applicants submit that this would be understood by a person skilled in art as sucralose which is purified as much as possible from impurities arising from its method of production. Since, an absolutely pure form is not likely to

exist, and the degree of purity obtained by the several methods available in the art shall vary, a "substantially pure form" is a phrase which very accurately points to sucralose that has been subjected to one or more steps of purification after its synthesis. Nevertheless, to facilitate advancement of prosecution, the term "substantially" has been deleted from the claims.

It is further clarified that the method of direct drying or conventional drying will yield the same constituents of solids in the same proportion that are present in the liquid taken for drying, except the free liquid is removed and the final constitution of the composition is a solid form.

The Examiner has stated that specific drying method of ATFD is critical to the instant subject matter, and spray drying would not achieve drying of "substantially pure" liquid concentrate of sucralose, based on the teaching of Carolyn (e.g. that sucralose by itself decomposes at high temperatures, i.e. 125°C (column 1, lines 13-18) which are temperatures at which spray-drying is performed). Carolyn teaches that spray drying can be utilized when sucralose is combined with 50 weight percent maltodextrin, which raises the temperature at which sucralose decomposes to 145°C, making spray drying possible. However, spray drying of purified sucralose liquid concentrates is shown by Applicants. Specifically, wherein the syrup obtained from the isolation stage was mixed well with 3-5 volumes of mass of ethyl acetate, the mass was distilled at low temperature to remove 2-4 volumes of ethyl acetate resulting in a liquid product concentrate, the desired dry product was obtained from the liquid concentrate by,

amongst other methods, by spray drying the liquid product concentrate to obtain of the acetyl intermediate or the desired deacylated product. See, p. 22, lines 13 to 16, WO2005/090374. The solid product could be also isolated by feeding the ethyl acetate extract after column chromatography (isolated / purified sucralose) directly into the spray dryer. See, p. 23, lines 20-23, WO2005/090374. Spray drying of pure sucralose was achieved both in ethyl acetate and water. The inlet and outlet temperatures inside the spray dryer to accomplish the spray drying operation were different when the ethyl acetate solution was spray dried and when water solution was spray dried. The flow rate of the feed was adjusted in such a way that the exposure of the feed to higher temperatures was only for few seconds and the drying took place within that time. Thus, the claimed subject matter is properly enabled for any method of direct drying (including spray drying) having conditions mild enough to prevent degradation or modification of chlorinated sucrose, for recovery of solids from the liquids such that the end product of such operations is a solid mass of the chemicals visibly free from the liquid, is a free-flowing powder and at least a part of which has particles that are amorphous or noncrystalline. Further, Carolyn, on account of their observations that spray drying cannot be applied to sucralose due to unstability at 125°C, leads a person skilled in the art away from use of spray drying as a technique for achieving separation of sucralose from its liquid concentrates. Hence, the instantly claimed subject matter is properly enabled by the instant specification for at least these reasons. The Examiner is respectfully requested to withdraw this rejection to the claims.

Furthermore, regarding the Examiner's comment that the instant claims do not preclude the mixing of sucralose with other additional ingredients prior to direct drying, Applicant clarifies that claim 26 recites a "process of handling solution of sucrose intermediates and derivatives, including, chlorinated sucrose"; in absence of a transition term "comprising" after the phrase "process of handling solution" is already restricted to "sucrose intermediates and derivatives, including, chlorinated sucrose" and, therefore does not include addition of any other chemical except for the associated impurities of the process of production. However, solely to advance prosecution, claim 26 has been amended to recite "A process of handling solution consisting of sucrose intermediates and derivatives, including, chlorinated sucrose with or without impurities..." Thus, mixing of sucralose with additional ingredients that would not be normally associated as impurities is precluded from the claim.

Still further, an essential element of claim 26 is "the liquids being obtained in a process of producing chlorinated sucrose, mainly 1',6' Dichloro-1',6'-Dideoxy- β - D-Fructo-Furanosyl-4-Chloro-4-Deoxy- α -D-Galactopyranoside" thereby excluding the presence of any chemical compound not derived from the process of production of sucralose. As noted above, the composition taught by Carolyn cannot be viewed as commensurate with the solids obtainable by the process of drying of claim 26.

Applicants have amended claim 50 to delete the phrase "directly from a process of crystallization".

Application of the eight factors described in *Re Wands* reveals that there is an adequate disclosure of the instant subject matter, adequate direction and guidance is presented, working examples are also provided and no or a minimal experimentation is required to apply the direction or the guidance as well as those working examples to achieve the results claimed.

The instant subject matter provides that a process of isolating sucrose intermediates and derivatives, including, chlorinated sucrose with or without impurities, from their liquid solutions by direct drying. It presents direction and guidance that this is possible under conditions mild enough to prevent degradation or modification of chlorinated sucrose. The specification provides working examples on both the types of mild conditions under which degradation or modification of chlorinated sucrose can be prevented, i.e. (1) achieving drying under low temperature, using ATFD drying under low temperature as well as low pressure, and (2) achieving rapid drying at brief exposure at high temperature by spray drying, the exposure being brief enough to prevent degradation or modification of chlorinated sucrose. There could be several different ways in which above two principles can be applied. Illustration of one working example of each of the above two principles shall provide enablement over the entire scope of principle of drying under mild conditions. There could be several variants of above two processes such as fluidized bed drying, application of which would only be question of routine experiments. With illustration of above two working examples, a person skilled in the art would not need to experiment to achieve sucralose isolation

from liquid concentrates by drying and the instant specification is enough to enable anyone to achieve the claimed results.

Regarding derivatives of sucralose, physical properties and thermal sensitivity of this group of sucralose derivatives are closely similar to each other and unless any unexpected property is shown to exist for any of sucralose derivative on account of which they will not be amenable to drying under mild conditions of drying, the instant process would not need undue experimentation. Applicants have shown working examples for sucralose, as well as sucralose-6-acetate. Sucrose-6-acetate, although not shown by example, does not have a property that suggests it will not get dried in ATFD or a spray dryer or an alternative direct drying method under mild conditions.

When seen in the context of *Genentech*, 108 F.3d at 1366, Applicants have claimed a process of isolating sucrose intermediates and derivatives, including, chlorinated sucrose with or without impurities, from their liquid solutions by direct drying, which is not a vague intimation of a general idea that may or may not be workable, but have given an enabling disclosure also of the same by working examples of the ATFD and spray drying on drying of reaction mixtures containing sucralose-6-acetate or sucralose with various degrees of purity.

Thus, all the *Wands* factors are satisfied to justify the breadth of claims since Applicants have provided information sufficient to practice the claimed subject matter for

drying pure sucralose. See, p. 22, lines 13-20 and p. 23, lines 20-22, both of WO 2005/090374.

For at least these reasons, the instantly rejected claims are properly enabled and the Examiner is respectfully requested to withdraw the rejections under 35 USC S. 112, first paragraph.

B. Second Paragraph

In the Action, the Examiner has rejected claims 48-53, 57 and 58 as being indefinite.

Applicants traverse this rejection.

Applicants have clarified herein that the drying process does not lead to any formation of derivatives or intermediates and that the drying process can be applied to sucralose or its derivatives or intermediates. It is true that only sucralose and sucralose-6-acetate are illustrated as examples of drying methods. However, as clarified in this specification, the instant subject matter is not limited to the particular methodologies, protocols, solvents, and reagents, etc., described herein as tools to achieve the claimed objective, as these may vary with a change in context. Thus, sucralose-6-acetate may, in an alternative process of sucralose production not illustrated here, be converted to sucralose penta acetate, crystallized out in pure form and deacetylated to produce sucralose. This has properties for drying much the same as sucralose and sucralose-6-acetate and may be dried applying the method of the instant claims.

The Examiner is correct in pointing out that page 21 recites incorrect names of

the compounds produced since inadvertently, β and α got replaced with atypical characters. Correct chemical name of sucralose is 1',6' Dichloro-1',6'-Dideoxy- β - D-Fructo-Furanosyl-4-Chloro-4-Deoxy- α -D-Galactopyranoside. The same corrections are necessary for these two symbols in the name of sucralose-6-acetate.

Claim 57 is deleted rendering the rejections thereto moot.

Regarding claim 50, the phrase "directly from a process of crystallization" has been deleted. However, the remaining features of the claim are correct, since the result of the process of drying in that claim is microcrystalline particles.

Claim 49 has been amended to keep only the broad limitations and narrow limitations have been deleted and made subject matter of new claim 59.

In view of above, withdrawal of the rejections under 35 U.S.C. §112, second paragraph is respectfully requested.

III. Rejection under 35 U.S.C. §102(b)

The Examiner has rejected claims 48-53 and 58 as being anticipated by Song et al., in U.S. Patent No. 5,227,182.

Applicants traverse this rejection. The cited reference fails to teach each and every element of the instantly rejected claims.

The test for anticipation is whether each and every element as set forth is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP § 2131.

The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP §2131. The elements must also be arranged as required by the claim. *In re Bond*, 15 USPQ2d 1566 (Fed. Cir. 1990).

Applicants respectfully direct the Examiner's attention to the fact that Song does not disclose a solid form of sucralose that is agglomerated. Instead, Song teaches "a mixture of sucralose and an agglomerating material". Applicants submit that it is clear that it will not be identified as sucralose. Agglomerating material is an entity that is an external addition. The process of Song is also not a process of isolating sucralose from its solution in liquid by direct drying. Rather, Song teaches formation of agglomerate of sucralose and sucralose derivative as intermediate step and formation of chewing gum as the final product. The material ground by Song is not sucralose but a mixture of sucralose and agglomerate; this is not "sucralose" or its derivative or an intermediate according to the instant subject matter. Song do not teach sucralose but a mixture of sucralose and cellulose derivative agglomerate which can be dried and added to chewing gum. See, claims 1, 7 and 18. Hence, the contention of the Examiner that the products of Song are identical or sufficiently similar to the compositions of claim 48 or inherently possess the instantly claimed physical properties has no basis.

In contrast, the instantly claimed subject matter pertains to sucralose or their derivatives or intermediates and not their mixture with another chemical entity. Further, the identity of the product made by drying of sucralose with maltodextrin in Song is not

sucralose. Hence, Song's product in no way teaches either inherently or expressly production of sucralose or its derivatives or intermediates by direct drying.

Furthermore, as clarified by the Examiner, the Merriam-Webster Online Dictionary defined "derivative" as "a chemical substance related structurally to another substance and theoretically derivable from it."

Additionally, the product of Song is not a solid powder form of sucralose. Therefore, there is no reasonable probability that it is either identical or sufficiently similar to the composition in claim 48 since the product of claim 48 has not been at all disclosed by Song.

For at least these reasons, the Examiner is respectfully requested to withdraw this rejection to the claims.

IV. Rejection under 35 U.S.C. §103(a)

The Examiner has rejected claims 48-53, 57 and 58 as being obvious over Song (above) in view of Jackson, in EP No. 255,260 and Kabbani, in U.S. Patent No. 6,646,121.

Applicants traverse this rejection. The Examiner has failed to make a *prima facie* case of obviousness against the instantly rejected claims based on the combined teachings of the cited references. It is submitted that a *prima facie* case of obviousness has not been established because nothing in the applied references teach or suggest all of the elements of the present claims, as required by *In re Wilson*.

To establish a *prima facie* case of obviousness, the Examiner must satisfy three requirements. First, as the U.S. Supreme Court very recently held in *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 (2007), “a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.” (*KSR, supra.*) Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

Song do not teach that a sucralose solution can be dried independent of a cellulose derivative agglomerate. Thus, Song fails to motivate a person skilled in the art

to produce an amorphous form of sucralose by direct drying of the liquid solution of sucralose according to the instant subject matter. In fact, the hygroscopicity of uncrystallized liquid concentrate of sucralose in water, which could be handled prior to the development of the instant subject matter only as crystals, teaches away from drying its liquid. Agglomeration of the same with a cellulose derivative actually is meant to circumvent that problem and does not achieve a solid powder sucralose that can be added to chewing gum. Jackson, despite knowing about formation of hygroscopic glass from sucralose, and despite knowing that small particles size sucralose is stable, chose to get the same by first crystallizing the sucralose out as long needle shaped crystals and then jet milling them to get a small stable particle form. Had achieving an amorphous form by direct drying been obvious to Jackson as a practical method of arriving at a solid powder form having a smaller particle size, as well as low residual moisture content and a stable form of sucralose, Jackson would have done it as a less cumbersome way of getting stable powder of sucralose__- at least as one more alternative way of getting stable sucralose powder of small particle size and low moisture content. Instead, Jackson has extensively taught the difficulty in achieving very small particle size by mechanical grinding, and that it is possible only through jet milling. Jackson then provides a method of enhancing the thermal stability of crystalline sucrose comprising jet milling to reduce the particle size and the size distribution.

Kabbani, in 2001, also worked with crystalline sucralose to prepare nonhydrous crystalline sucralose of low residual moisture content rather than attempting to get an

amorphous form of sucralose with a low residual moisture content as an alternative for crystalline sucralose.

Looking at the complex technological solutions taught by Jackson and Kabbani, the instant matter, i.e. an amorphous form of sucralose, provides a solution to the long standing problem of stability of sucralose which is surprising and simple. This shows that for Jackson, as well as Kabbani, who are persons skilled in the art, making amorphous form of sucralose was not obvious to them as viable or at least as an additional way of getting stable solid sucralose, although the principle objective of both teachings was to achieve sucralose of improved storage stability. What was not at all in the contemplation of and that was not obvious to Jackson in 1987 and to Kabbani in 2001, cannot be considered as an obvious suggestion to the Applicants. Jackson and Kabbani failed to comprehend or predict an amorphous form as a feasible solution to the long standing problem of stability of sucralose.

The fact of absence of amorphous form in the teachings of Jackson and Kabbani as at least an alternative solution to / for getting stable sucralose supports that the knowledge alone, which was available to Jackson as well as Kabbani, that small particle size or/and low residual moisture content give stability to sucralose is not a motivating factor that obviously leads a person skilled in the art to produce an amorphous form. In fact, neither production of amorphous form nor its small particle size and low residual moisture content was the initial objective of Applicants and these findings came as surprising and unexpected results of the success in drying the liquid concentrates of

solutions of sucralose. The problems identified in sucralose manufacture and sought to be solved by the instant subject matter are discussed in detail on pages 1 to 4 of the instant specification. Interference of tertiary amide in post-chlorination steps of isolation and recovery of sucralose by solvent extraction as well as crystallization is a well known and long standing problem in sucralose manufacture, which was intensively investigated and solved by Navia et al. (1996) in U.S. Patent No. 5,498,709 by steam distillation. However, due to the fact that tertiary amide is a high boiling solvent, it takes a very long time for it to be stripped off to the maximum limits and, in the process, volume of the mass increases to 4 to 5 times of the original volume. This increase in volume also increases the time for isolation of the product, as well as increases size of the processing plant to that extent for handling the resultant volume of reactants for further processing. Crystallization processes are cumbersome.

A batch process, as described by Mufti et al., in U.S. Patent No. 4,380,476 besides being cumbersome, results in loss of uncrystallized sucralose. A continuous crystallization process of Navia et al., in U.S. Patent No. 5,498,709 (the number given wrongly as 5,498,706 in the specification) requires additional equipment, is more cumbersome to operate and does not totally prevent loss of uncrystallized sucralose. On this background, as explained on pages 3 and 4 of the instant specification, the objectives were (a) making post chlorination steps more efficient by achieving total removal of tertiary amide from reaction system in a most convenient and most efficient way in very short time with –much smaller volumes to be handled in post-chlorination

steps reaction mixture, and (b) achieving isolation of all the sucralose derivative or sucralose formed in one single step of drying without the need of cumbersome crystallization by a batch process or continuous mother liquor recirculation process. Drying was sought to be achieved as most convenient, more effective and more efficient alternative to batch or cumbersome continuous processes of crystallization described by U.S. Patent No. 4,380,476 and Navia et al., in U.S. Patent No. 5,498,709. The finding of the final powder of the product or product intermediate obtained by drying process as being amorphous in nature and non crystalline, which was free flowing and had better stability was totally an unexpected and surprising result even for the Applicants themselves.

MPEP §2141 provides guidance based on *Graham v. John Deere Co.*, 383 U.S. at 17, 148 USPQ at 467 that an investigation is necessary to find out what would be obvious to a person of an ordinary skill in the art at the time the invention was made. If the factual inquiry reveals that the invention claimed could not have been obvious to a person of an ordinary skill in the art, the *prima facie* case of obviousness can not be sustained and must be withdrawn.

MPEP §2141.03 provides guidance on how to determine a person of an ordinary skill in the art. It states that "The examiner must ascertain what would have been obvious to one of ordinary skill in the art at the time the invention was made, and not to the inventor, a judge, a layman, those skilled in remote arts, or to geniuses in the art at hand. *Environmental Designs, Ltd. v. Union Oil Co.*, 713 F.2d 693, 218 USPQ 865 (Fed.

Cir. 1983), cert. denied, 464 U.S. 1043 (1984).” In this context, Jackson and Kabbani are not merely persons of ordinary skill in the art but are even the pioneers in the art who failed to predict that an amorphous form will have the properties of a stable sucralose which were sought.

For at least the above reasons, Applicants submit that a *prima facie* case of obvious has not be establish by the cited combination of references, and the Examiner is respectfully requested to withdraw this rejection.

V. Provisional Rejection under Nonstatutory Double Patenting

The Examiner has provisionally rejected claims 48-53 and 58 as being unpatentable over claims 1, 2, 8 and 9 of U.S. Patent Application No. 12/225,378. Applicants respectfully submit that this rejection will be address at such a time as there is an indication of allowable subject matter in this or the co-pending subject matter. Therefore, the Examiner is kindly asked to hold this rejection in abeyance.

CONCLUSION

The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

THE NATH LAW GROUP

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THE NATH LAW GROUP
112 South West Street
Alexandria, VA 22314
Telephone: (703) 548-6284
Facsimile: (703) 683-8396

/Tanya E. Harkins/
Joshua B. Goldberg
Reg. No. 44,126
Tanya E. Harkins
Reg. No. 52,993
Customer No. 20529